Name _____

# Karyotyping with Magnetic Chromosomes

## Introduction:

Human beings have a total of 46 chromosomes: 22 pairs of autosomes and 1 pair of sex chromosomes. One member of each human chromosome pair is inherited from the mother (maternal) and the other from the father (paternal). These maternal-paternal chromosome pairs are referred to as homologs, or homologous chromosomes. Human gametes (egg and sperm cells) are produced through meiotic division, a process that divides the number of chromosomes in half, so that each gamete carries 23 chromosomes. These chromosomes comprise one member of each homologous pair. During fertilization (the union of egg and sperm), these gametes combine to restore the total number of chromosomes to 46.

Normal human gametes carry one member of each homologous chromosome pair. However, errors occasionally occur during meiosis that create gametes with an improper number of chromosomes (numerical abnormality) or with an irregular chromosomal structure (structural abnormality). When such gametes participate in fertilization, they usually produce either nonviable embryos or offspring with disorders resulting from the chromosomal abnormality. Most chromosomal abnormalities arise from errors occurring during meiosis.

Numerical chromosomal abnormalities result from an incorrect distribution of chromosomes into the gametes during meiosis. This can happen when homologous chromosomes (maternal and paternal chromosome copies) fail to separate during Meiosis I, or when sister chromatids (duplicated chromosome copies joined at the centromere) fail to separate during Meiosis II. This lack of chromosome separation is called nondisjunction and it results in some gametes having two copies of a particular chromosome and some gametes without any copies (see Figure 1). Figure 1 traces the meiotic division of one homologous chromosome pair; however, humans have 46 total chromosomes and nondisjunction can occur for any autosome or sex chromosome.

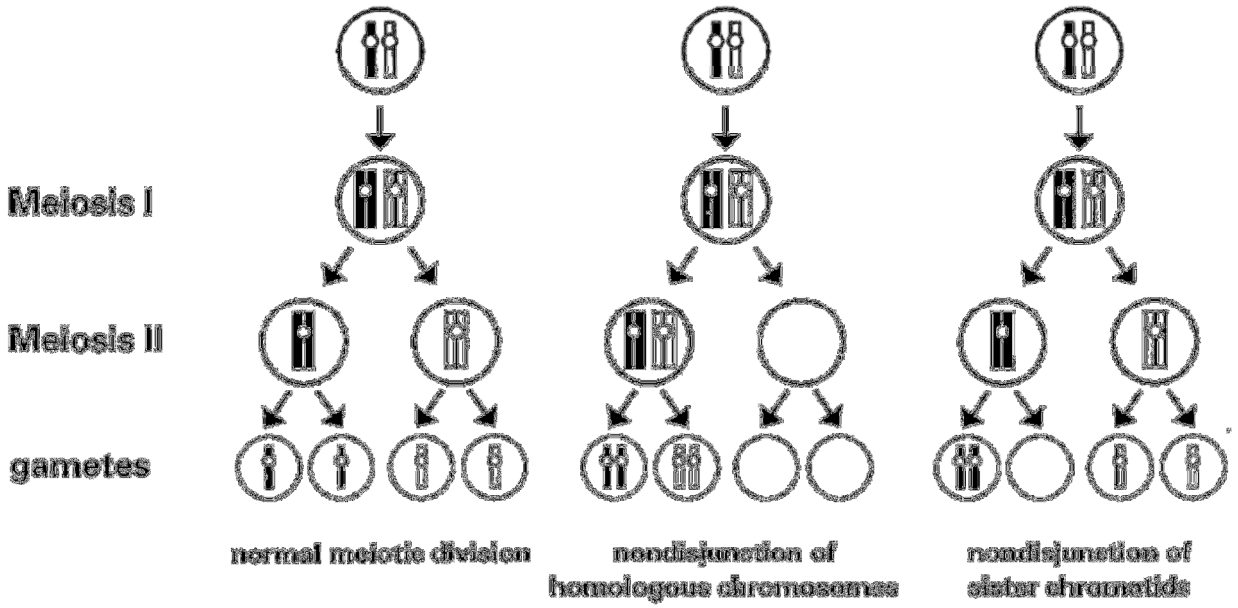


Figure 1. Normal Meiosis and Meiotic Nondisjunction
Black represents paternal chromosome. White represents maternal chromosome.

When gametes with an extra chromosome are joined with a normal gamete at fertilization, they produce zygotes with three copies of that chromosome. This creates a condition known as trisomy. When nondisjunction leads to three copies of Chromosome 21, the resulting trisomy (trisomy 21) causes Down's syndrome in live births. Trisomies of sex chromosomes can also produce viable offspring. For example, males possessing one extra X chromosome have a condition known as Klinefelter's syndrome. These males are taller than average, may have reduced intelligence, and are usually sterile.

As a general rule, the human body can tolerate excess genetic material more readily than it can tolerate a deficit of genetic material. Therefore, deletions of entire chromosomes, called monosomies, usually result in miscarriage. Monosomies of all autosomes, with rare exception, are lethal. However, monosomy of the X chromosome, known as Turner's syndrome, can produce viable offspring. Individuals with Turner's syndrome are female, are usually less than five feet tall, have webbing of the neck, do not develop underarm or pubic hair, and have underdeveloped ovaries.

The study of chromosomes, chromosomal abnormalities, and related diseases is called cytogenetics. In this activity, you will act as a cytogeneticist by using magnetic chromosomes to create a human karyotype. A karyotype is a visual, ordered display of all of the chromosomes from one somatic cell (a body cell, excluding egg and sperm) of an individual. Karyotypes are created using condensed, duplicated chromosomes that have been arrested in metaphase of mitosis using colchicine, a drug that inhibits mitosis. The use of colchicine is critical to karyotype preparation. In non-dividing cells, chromosomes look like long, stringy fibers that bunch together within the nucleus like a ball of cotton. Individual chromosomes are not distinguishable. However, during mitosis (cell division), each chromosome condenses and becomes visible as a separate entity. Colchicine freezes the chromosomes during a stage where they are easily visualized individually. The chromosomes are then dyed with Giemsa stain (or other dyes) to create distinctive banding patterns on each chromosome pair. The stained chromosomes are spread out on a slide and photographed through a microscope. The resulting array of chromosomes is called a metaphase spread.

Non-homologous chromosomes differ in size, centromere position, chromosome arm length, and staining patterns, and they are identified based on these characteristics. Chromosomes are classified as one of three types based upon the position of the centromere. The three types are metacentric, submetacentric, and acrocentric. Each chromosome strand extending form the centromere is referred to as an arm. A metacentric chromosome has a centromere that lies near the middle of the chromosome. Therefore, the arms of metacentric chromosomes are of approximately equal length. A submetacentric chromosome has a centromere that lies off-center, somewhere between the middle and the tip of the chromosome. This makes one arm noticeably shorter than the other. The short arm is labeled *p* (for petite) and the long arm is labeled *q* (simply because "q" follows "p" in the alphabet). An acrocentric chromosome has a centromere that lies near the tip of the chromosome. This causes the petite arm to be extremely short.

Homologous chromosomes have the same banding pattern, centromere position, arm length, and overall size. By careful analysis of chromosome morphology, cytogeneticists match pairs of homologous maternal and paternal chromosomes from the metaphase spread. In a karyotype, chromosomes are displayed in homologous pairs approximately from largest to smallest (1-22) and they are, by convention, aligned with the short arm oriented on top. Chromosomes are also arranged in groups (A through G) according to common physical features (similar size and centromere position). The groups are separated slightly when laid out in a karyotype display. The sex chromosomes do not have a lettered group name and are traditionally located in the lower, right-hand corner of the karyotype.

Instructions:

*You will receive a metaphase spread of magnetic chromosomes and a magnetic layout board. Follow the instructions below to identify each chromosome, identify homologous pairs, and arrange the pairs to create a karyotype. Then, determine the genetic makeup, gender, and chromosomal disorder indicated by the karyotype. Refer to the Chromosome Key on the last page as needed.*

1. Remove the magnetic chromosomes from the bag and spread them out face up on your desk. This represents a spread of metaphase chromosomes dyed with Giemsa stain from which cytogeneticists piece together an individual's karyotype.
2. Choose a magnet. Compare it to the chromosome key and identify which chromosome it represents. Look carefully at distinguishing characteristics such as chromosome size, centromere position, length of chromosome arms, and G-banding pattern.
3. Once you have identified the chromosome, place it on the magnetic layout board, just above the short, solid line with the chromosome's number (or letter, for sex chromosomes) below it. Line up the centromere with the long, dashed, horizontal line.
4. Search the chromosome spread to find the homologous pair for the chromosome that you identified. Homologous chromosomes are identical in size, centromere position, chromosome arm length, and banding pattern.
5. Place this magnetic chromosome beside its homolog on the magnetic layout board.
6. Arrange all of the magnetic chromosomes in this manner until you have identified, placed, and matched all of the chromosomes, and the karyotype is complete. Keep in mind that this karyotype reflects a chromosomal abnormality.
7. Fill in the table below to help you determine the type of chromosomal abnormality.
8. Use the information in the introduction to answer the questions on the next page.

| Letter on Bag | Total # of Chromosomes | Sex Chromosomes | Gender | Extra or Missing Chromosomes? (Which one?) | Type of Chromosomal Disorder |
|---|---|---|---|---|---|
| | | | | | |

**Review the Introduction to Answer the Following Questions:**

1. How many total chromosomes do each of the following normally have?
    - Human gametes (egg or sperm)
    - Human zygotes (fertilized egg)

2. Abnormalities in the number of chromosomes results when chromosomes are not correctly distributed into gametes during meiosis. This can happen when homologous chromosomes fail to separate during _____ or when sister chromatids fail to separate during _____. This lack of chromosome separation is called _____.

3. If nondisjunction occurs in humans for one pair of homologous chromosomes during Meiosis I (compare first diagram with second diagram on front page):
    - How many of the 4 gametes are normal?
    - How many of the 4 gametes will have an extra chromosome?
    - How many of the 4 gametes will be missing a chromosome?

4. If nondisjunction occurs in humans for sister chromatids of one chromosome during Meiosis II, (compare first diagram with third diagram on front page):
    - How many of the 4 gametes are normal?
    - How many of the 4 gametes will have an extra chromosome?
    - How many of the 4 gametes will be missing a chromosome?

5. If a human gamete with an extra chromosome participates in fertilization with a normal human gamete:
    - What condition results?
    - Three copies of chromosome 21 results in what syndrome?
    - An extra X chromosome in males results in what syndrome?

6. If a human gamete that is missing a chromosome participates in fertilization with a normal human gamete:
    - What condition results from this deletion of a chromosome?
    - In most cases, what happens if an autosome is missing?
    - A missing copy of an X chromosome in females results in what syndrome?

7. Refer to the chromosome key or the completed karyotype display that you assembled. How is the centromere positioned on Chromosome 1 vs 9 vs 14?
   (ie-Which is metacentric vs acrocentric vs submetacentric?)
    - Chromosome 1
    - Chromosome 9
    - Chromosome 14